50 years of double helix:

Genetic engineering: living on a Flat Earth!

GE – based on old-fashioned ideas

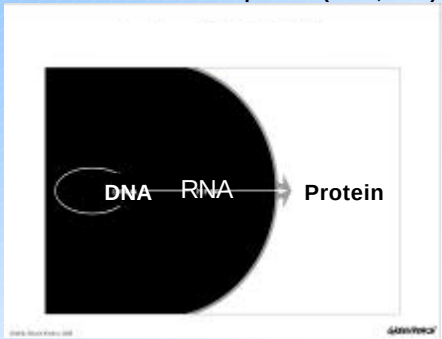
- Genetic engineering relies on the principles that proposed to explain DNA function in the 195Os, very soon after the discovery of the DNA structure.
- But there have been many discoveries on the nature of DNA since then and the view (or paradigm) of gene function has changed dramatically.
- Genetic engineers refuse to believe that their beliefs are old fashioned and their techniques crude. Like people living before the 15th century, before they knew the Earth was round, they are living on a flat earth.

The Central Dogma of Molecular Biology

- A "Dogma" is a belief or doctrine.
- First proposed in the 1950s to explain the function of DNA.
- States that DNA makes proteins through RNA.
- DNA codes for genetic information. No genetic information can be transferred back to DNA.
- Very simplistic model

The Central Dogma

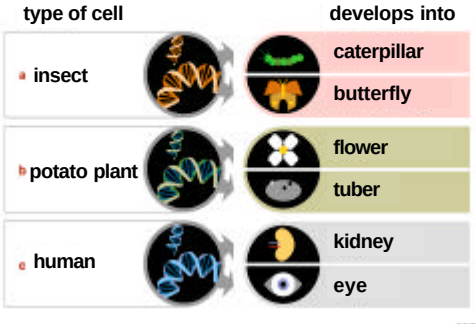
DNA makes RNA makes proteins (Crick, 1958)



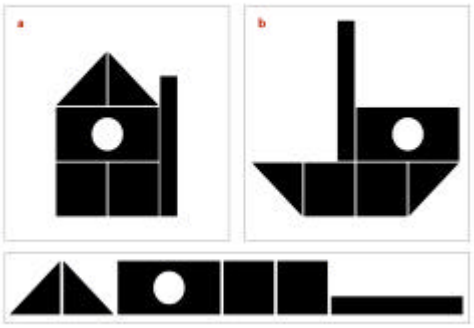
What is a gene?

- DNA is arranged in an "alphabet", a genetic code for the production of proteins through RNA.
- In the 1960's, the code was deciphered and genes were thought of as this code.
- But, there is more to genes than a code for proteins. Genes perform many functions, but must be controlled and regulated in order to do so.

Organisms or parts of organisms with identical genes can produce very different forms.



The same elements - different results



Genes need to be regulated

- Genes need to be told to switch “off” and “on”.
- Genes need to be told how much expression (protein) is required and where.
- Genes need to be regulated – this regulation is not performed by DNA but by many other controls arranged in a complex network.
- “*In order to assemble that meaningful story, a living cell uses a second informational system. (...) The key concept here is that these dynamic epigenetic networks have a life of their own — they follow network rules not specified by DNA.*”

Strohman , April 2001
California monthly, A new paradigm for Life, Beyond genetic determinism.

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Networks regulating genes

- There are many ways in which gene expression can be regulated. The full picture of how genes are regulated is still being studied, but it is thought that these factors are part of a hierarchical, complex, network.
- “Transcription factors”: proteins which interact with regions of the DNA to switch genes on.
- Interference RNA: a recent discovery. A new type of RNA that, instead of making proteins, stops gene expression at the RNA level. Thought to give protection of genome against viruses.
- Gene silencing: genes can be switched off and this can be an inheritable trait, although there are no changes to the DNA (epigenetic traits). It is not known exactly how this happens.

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More regulatory networks: evidence from the human genome

- The DNA sequence of the human genome was published in 2001.
- The big suprise was that a human being has only about 30,000 –40,000 genes and not 100,000, as had been assumed.
- These genes encode a high number of different proteins – how do they do this?

Craig Venter (leading scientists of the human genome project):
“*This tells me that genes can’t possibly explain all of what makes us what we are.*”

Venter, 2001, Science 291, 1304 Human Genome Project, 2001

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Many proteins from so few genes – more evidence for gene regulation

- Genes encode a high number of proteins, because the genetic code is an alphabet, not an essay.
- A gene consists of many different parts which can be put together in different ways (alternative splicing) to produce different proteins.
- Also, some proteins are formed, but then cut down to the right size.
- All these mechanisms need tight control – by a regulatory network.
- “*DNA has been called the Book of Life by the Human Genome Project scientists, but many other biologists consider DNA to be simply a random collection of words from which a meaningful story of life may be assembled.*“

Strohman, April 2001, California monthly, a new paradigm for Life, Beyond genetic determinism.

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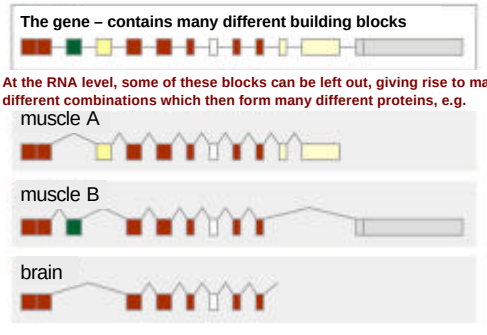
Alternative splicing – a rough guide



DNA structure affects gene expression

- DNA is coiled and coiled again to pack tightly into chromosomes.
- It is now thought that this coiling changes with time and controls gene expression.
- The position of the gene on the chromosome is an important factor regulating gene expression or not.
- Modifications to the "beads" (histones) that the DNA is wrapped round can also control gene expression.
- Controls over the DNA structure are needed. Part of the regulatory network.

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The type of surroundings also affects gene expression

Gene expression is dependent on their surroundings, the type of cell they are in:

"Genes never act in isolation; their effect is determined (in part) by the genetic background and the environment."

Pickardt, T., 2002

This means even more regulatory control of gene expression!

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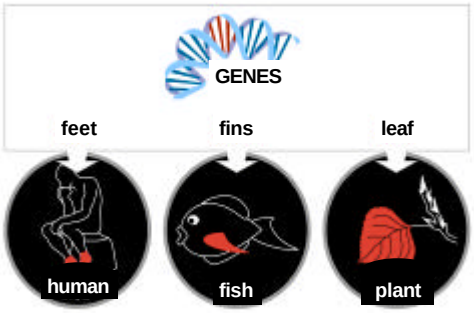
The expression of genes depends on their surroundings



How are genes viewed now?

- The discoveries of gene regulation mechanisms prove the Central Dogma to be an over-simplistic complex of how genes function.
- Many different mechanisms for gene regulation have been discovered. This has caused a "paradigm shift", a major change in our thinking of how genes function. There is, as yet, no overall picture of the genetic regulatory network.
- Science is just beginning to appreciate how complex such a network would be.

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How does this affect genetic engineering?

- GE does not consider any gene regulatory network
- GE relies on the Central Dogma, now viewed as "over simplistic".
- GE assumes one gene equals one function.

GE relies on outdated science

The GE industry lives on a flat earth!

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GE is crude technology, because:

- it deliberately interrupts and violates the tightly controlled network of DNA
- it alters genetic information and the expression of genes
- it eliminates cell's ability to self-regulate its function
- it is not possible to control the place where the gene is incorporated, the number of copies that are incorporated, or the effects of its interaction with other genes.
- the often forcible insertion of DNA into a tightly controlled genetic regulatory network is **likely to produce unintended effects**.

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GE is crude technology

"In most cases of plant modification, DNA insertion takes place at random, unpredictable loci. Such random insertion may lead to unintentional changes in gene expression."

OECD (2000) Report of task force for the safety of novel foods and feeds (C(2000)86/ADD1)

No wonder there are so many unexpected effects with GE organisms!

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An example of crude technology: the gene gun

- The "gene gun" is used to genetic engineer plants. Many commercialised plants produced by Monsanto use this technology.
- It fires particles coated with DNA at cells. The DNA is inserted at random.
- Fragments of the genetic insert are often included along with complete copies. Rearrangements of the plant's DNA occur frequently.
- Some of these effects have only become known after the GE crop has been grown in the environment and eaten by animals and humans (e.g. Roundup Ready Soya).

It's like firing a shotgun at the plant genome!

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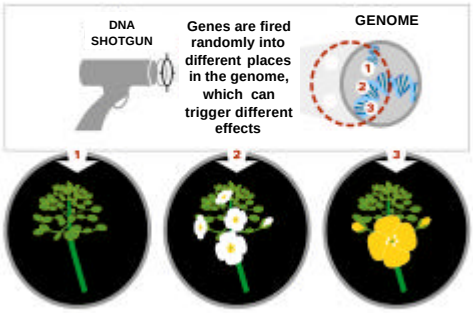
Gene transfer in shotgun process



Unexpected effects are common in genetically engineered organisms

- The following slides give examples of the many documented unexpected effects produced by the genetic engineering of organisms. Some of these GE organisms are grown commercially, e.g. in the USA.
- Unexpected effects occur with all GE technologies, including the gene gun technology.

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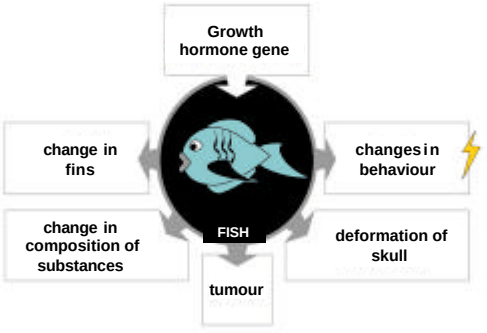
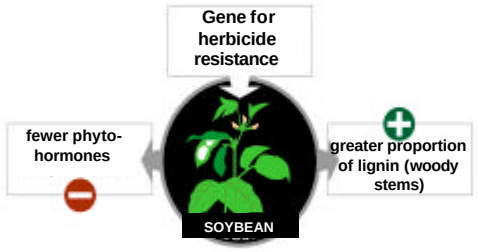
Unexpected effects: GE yeast

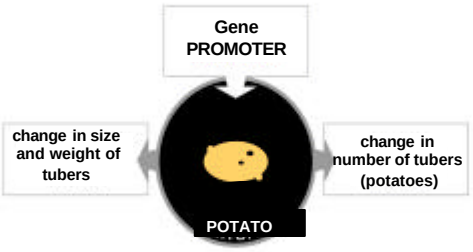
Unexpected effects: GE fish



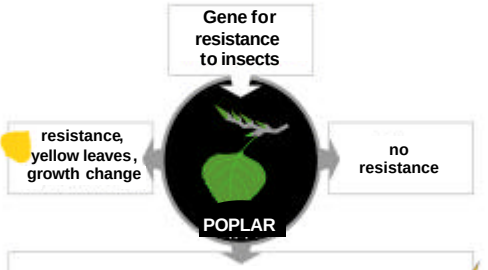
Unexpected effects: GE Soybean



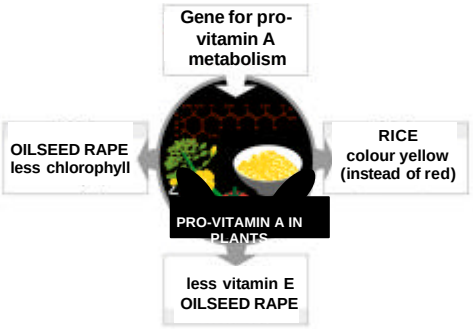
Unexpected effects: GE Potato



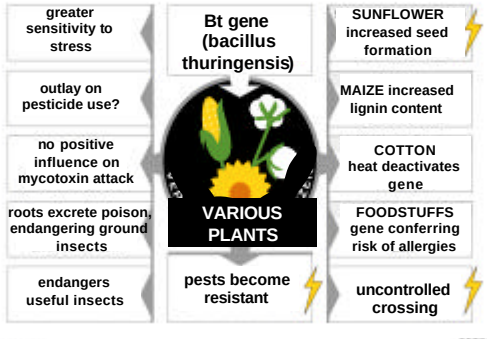
Unexpected effects: GE Poplar trees



Unexpected effects: GE plants for vitamin A



Many possible effects caused by the insecticidal Bt gene



Unexpected effects – possible consequences

- **GE can produce new toxic substances by:**
  - –interrupting detoxifying processes,
  - –activating new toxic processes,
  - –interfering in the complex secondary metabolism of plants.

? food safety is unknown.

? ecological risk is unknown. It is not known how such substances interact with other organisms, e.g. plants become particularly prone to pests or become toxic to beneficial insects.

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Summary

- Genetic engineering is a crude and old fashioned technology.
- GE relies on the outdated Central Dogma of molecular biology which is 50 years old.
- GE disregards all the new knowledge on gene regulation.
- GE is not compatible with the complex regulatory systems that control gene expression
- GE commonly gives rise to unexpected effects, with unknown implications to the environment or food safety.

THE GE INDUSTRY ARE LIVING ON A FLAT EARTH!

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Conclusions on the release of GMOs to the environment:

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